Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Virology

Editorial overview: Preventive and therapeutic vaccines

Marc HV Van Regenmortel

Current Opinion in Virology 2018, **29**:xx–yy

https://doi.org/10.1016/j.coviro.2018.03.002

© 2018 Published by Elsevier B.V.

Marc HV Van Regenmortel

School of Biotechnology, University of Strasbourg, Boulv Sebastien Brandt, Illkirch 67410, France
e-mail: vanregen@unistra.fr

Marc HV Van Regenmortel is an Emeritus CNRS Research Director at the School of Biotechnology of the University of Strasbourg, France. He was Director of the Immunochemistry Laboratory at the CNRS Molecular Biology Institute in Strasbourg (1979–2002) and professor of Virology at several Universities in South Africa and France (1967–1978). He has published 400 research and review papers as well as a dozen books in Immunochemistry and Virology. He is Editor-in-Chief of Archives of Virology and Journal of Molecular Recognition and Associate Editor of Advances in Virus Research, Analytical Biochemistry, Frontiers in Immunology, Journal of Immunological Methods and Bionomina. His h-factor is 51.

During the last century many molecular biologists believed that biology would eventually be reduceable to chemistry although this is no longer believed today. It is also likely that molecular vaccinologists will in future discard the assumption that it is possible to develop effective vaccines against viruses solely on the basis of the atomic structures of their epitopes bound to neutralizing monoclonal antibodies.

In his book *Of Molecules and Men*, Nobel laureate Francis Crick [1] claimed: 'The ultimate aim of the modern movement in biology is to explain all biology in terms of physics and chemistry'. A reductionist mindset, indeed, leads to the expectation that biological systems can be fully described and understood in terms of the physico-chemical properties of their constituent parts [2]. The success of molecular and systems biology for dissecting the immune system (IS) has, for instance, accredited the view that both cell-mediated and antibody-mediated immunity will eventually be fully understood by studying the structure and activities of antigens, antibodies, B-cell and T-cell receptors, MHC molecules, cytokines and a few other components of the IS. Reductionists tend to overlook the fact that when they dissect the IS into its numerous constituent parts, they actually destroy crucial emergent properties which arise in these parts when the integrated system acts as a functional whole but which are absent when the parts are studied in isolation. Such a view makes it difficult, for instance to admit that the antigenic structure of an epitope bound to a monoclonal antibody (Mab) may differ from the immunogenic structure of the same conceptual epitope when it is bound to a B-cell receptor [3]. Reductionist thinking may also induce vaccinologists to assume that when an epitope present in HIV spikes binds to a neutralizing Mab (which is necessarily always polyspecific), the same epitope should also be able to induce similar neutralizing Abs when used for immunizing humans [4]. When they confound the chemical nature of antigens with the biological nature of immunogens, vaccinologists are led to believe that they are able to design an effective vaccine immunogen by using the strategy of structure-based reverse vaccinology [3], whereas they are in fact only improving the binding reactivity (i.e. the antigenicity) of a single epitope.

Physicists and chemists used to believe that the universe was ruled by mathematical laws that made it possible to predict the future behaviour of any system if one had an intimate knowledge of its initial conditions. In the twentieth century, the development of chaos theory by Henri Poincaré and Edward Lorenz made that assumption untenable because it was discovered that extremely small differences in the initial conditions of a dynamic system

Please cite this article in press as: Van Regenmortel MHV: Editorial overview: Preventive and therapeutic vaccines, Curr Opin Virol (2018), https://doi.org/10.1016/j.coviro.2018.03.002

had a huge impact on the subsequent state of the system. This makes it impossible to predict the system's future behaviour and explains, *inter alia*, why long term weather predictions (longer than a week) are not feasible in spite of our enormous, modern computational power [5].

Since making precise quantitative measurements of the innumerable initial conditions of a complex biological system is less feasible than with physical systems, it is evident that making accurate predictions about any future state of a dynamic biological system is going to be even more intractable. A further difficulty is that many of the problems faced by vaccinologists are so-called inverse problems which consist in trying to guess what are the possible causes of a wanted but hypothetical protective immune response. Trying to understand the past (i.e. the many causes that may have given rise to an effect) is actually more difficult than trying to predict the future because it excludes the possibility of simply waiting to see what happens when scientists try to solve direct problems in vaccinology by determining what are the effects that follow from certain causes [6]. The limitations posed by chaos theory obviously are even more intractable for solving inverse problems.

The use of Mabs for identifying which epitopes of a virus are plausible vaccine targets has the unfortunate consequence that vaccinologists are led to focus on discrete, single epitopes as potential immunogens instead of studying the clusters of overlapping epitopes that always collectively form a viral antigenic site. It is well-known most protective immune responses against pathogens correspond to polyclonal immune responses and that antigenic clusters present in the major epitopic regions of a pathogen are more likely to elicit a protective immune response than a single epitope identified with one Mab [7]. Concentrating one's attention on the interactions between single epitope–paratope partners does not provide the information one needs to control immune defence mechanisms that involve a large number of individual molecular participants. This complexity is responsible for our inability to predict molecular recognition events between biomolecules (including antigen–antibody reactions) even when the strength of individual hydrogen bonds involved in the overall reaction is exactly known [8].

The first contribution in this issue of Current Opinion in Virology by Adan Rios presents a new paradigm in HIV vaccine research which stresses that vaccinologists should pay more attention to the immune responses directed against the initial acute phase of HIV infection. It is remarkable that most published studies of neutralizing anti-HIV Mabs concern human antibodies that appear after several years of chronic HIV infection and which are usually unable to control HIV infection in the infected individuals from whom the Abs are obtained. It is also known that most heterosexually transmitted HIV infections are caused by a single, so-called transmitted/founder (T/F) virus which is not the predominant variant present in the donor [9]. Compared to viruses present in HIV chronic infection, T/F viruses have about twice more spikes per virion, have fewer N-linked glycosylation sites and are more efficiently captured by dendritic cells [10]. According to Rios, T/F viruses may hold the key for identifying possible immunogens that could lead to a protective HIV vaccine since it is the neutralization of viruses present at transmission that may be best able to prevent further viral dissemination [11]. After the virus has been integrated in the host genome, continuous changes in the antigenic properties of new virions appear, usually attributed to antibody affinity maturation by somatic hypermutation. The constant changes in virion immunogenic sites during chronic HIV infection that can be attributed to the error-prone activity of reverse transcriptase lead to a wider diversification of the induced Abs than would be expected from a genuine affinity maturation process that occurs when a single clone of B-cells drives the immune response towards the production of higher affinity Abs.

Recent confocal microscopy studies [12] have shown that when the virus enters its target cell, highly conserved epitopes become exposed, distal to cell–virus interfaces, which offer a window of opportunity for developing neutralizing Abs directed to T/F viruses. Rios also argues that the time-honoured method of chemical virus inactivation for developing human and veterinary vaccines should receive renewed attention because novel, entirely safe methods for irreversibly inactivating HIV inactivation are now available [13]. According to Jacob Bronowski: 'Science is the acceptance of what works and the rejection of what does not, which needs more courage than we may think'. This suggests that the experimental evaluation of a HIV vaccine based on inactivated T/F viruses is a project that deserves considerable attention.

The second contribution in this issue by Teresa de los Santos *et al*. provides a detailed analysis of the need for improved vaccines against foot-and-mouth disease (FMD). This is a worldwide and extremely contagious viral disease of domestic and wild cloven-hoofed animals that include cattle, swine, sheep, goat as well as giraffes. In view of its enormous economic impact, the importation of animal products from FMD endemic countries is strictly regulated and such countries need to acquire the status of FMD free zones if they want to participate in such type of international trade. The most successful and commercially available FMD vaccines that protect against the various serotypes of FMDV present in different countries consist of purified, chemically inactivated virus particles that have been depleted from contaminating viral non-structural proteins (NSPs) and are then formulated with adjuvants. Since this vaccine is heat

Please cite this article in press as: Van Regenmortel MHV: Editorial overview: Preventive and therapeutic vaccines, Curr Opin Virol (2018), https://doi.org/10.1016/j.coviro.2018.03.002

Download English Version:

https://daneshyari.com/en/article/8506533

Download Persian Version:

https://daneshyari.com/article/8506533

Daneshyari.com